REMARKS

Claims 1-10 and 13-24 were pending in this application when last examined. Claim 1 has been amended. Support for the amendments can be found in the specification and original claims as filed. No new matter has been added.

Support for claim 1 can be, for example, in paragraphs [0026] and [0031] as referenced in the patent application publication (US 2007/0110801 A1).

Applicants submit that this Amendment After Final Rejection places this application in condition for allowance by amending claim 1 in a manner that is believed to render all pending claims allowable over the cited art and/or at least place this application in better form for appeal. This Amendment was not earlier presented because Applicants believed that the prior responses placed this application in condition for allowance, for at least the reasons discussed in those responses. Accordingly, entry of the present Amendment, as an earnest attempt to advance prosecution and/or to reduce the number of issues, is requested under 37 C.F.R. §1.116.

CLAIM REJECTIONS - 35 USC § 102

At page 5, item 14, the Office Action rejects claims 1-8, 13-21 and 23-24 under 35 U.S.C. § 102(b) as being

anticipated by PANKHANIA et al. (WO 02/083119). Applicants respectfully traverse the rejection.

Currently amended independent claim 1 is directed to a composition to be buccally administered as a tablet or lozenge, comprising a low dosage lipophilic non-steroidal anti-inflammatory (NSAID) or anti-mycotic drug under an amino acid salt form, wherein the composition is formulated to be passively diffused into buccal and throat mucous membranes when the composition is totally released, dissolved, coated to the mucous membrane, and then absorbed through the mucous. PANKHANIA fails to teach or suggest such a composition.

PANKHANIA relates to a composition for treating migraine and nausea that includes ibuprofen and prochlorperazine. PANKHANIA discloses that the composition can be administered orally, rectally, parenterally, buccally or topically. Preferably the compositions are in a form "suitable for oral administration or in the form of a suppository." (See, page 4, lines 20-24).

PANKHANIA then describes compositions for oral administration, such as solid compositions (see, page 4, lines 32 to page 5, line 14) and liquid compositions (see, page 7, lines 9-17). PANKHANIA also describes compositions for topical administration (see, page 7, line 19 to page 8, line 2), rectal administration (see, page 8, lines 12-17), and parenteral administration (see, page 8, lines 19-21). Missing from

PANKHANIA, however, is any disclosure related to buccal administration. Thus, PANKHANIA is non-enabling with respect to the claimed subject matter.

MPEP § 2121.01 states that in order for a cited art document to anticipate a claim, the cited art must provide an enabling disclosure of the claimed subject matter. This section of the MPEP goes on to state that the mere naming or description of the subject matter is insufficient; rather, the cited art must demonstrate that the public was in possession of the claimed subject matter before the date of invention. In other words, the cited art must describe the claimed subject matter in such detail as to enable one of ordinary skill in the art to make the claimed subject matter without undue experimentation.

In the present case, PANKHANIA fails to enable one of ordinary skill in the art to make the claimed subject matter without undue experimentation. For instance, the composition of instant claim 1 is buccally administered and includes low dosages of lipophilic drugs formulated to be passively diffused into buccal and throat mucous membranes. Previous attempts at developing similar compositions have been difficult and PANKHANIA fails to teach or suggest anything to overcome these difficulties.

For example, it is known that lipophilic drugs are hydrophobic and insoluble in the mouth/saliva environment. As a result, the lipophilic molecules remain in the crystalline state

and do not dissolve; therefore, the active ingredient cannot be absorbed by the mucous epithelium. Moreover, the acid insoluble crystal forms induce nausea and local irritation when the drug comes in contact with mucous tissue.

Applicants have developed a composition wherein lipophilic compounds, such as nonsteroidal anti-inflammatory drugs and anti-mycotic drugs, can be buccally administered yet dissolve and remain stabilized while passively diffusing into the mucous membrane. While PANKHANIA mentions buccal administration, they fail to teach or suggest, or enable one to overcome the prior established problems.

At page 6, the Office Action states that "the composition taught by Pankhania can be retained in the oral cavity and since this composition contains all the structural components of the instant claims, the delivery of the active ingredient across the oral or buccal mucosa will necessarily occur." Also, at page 7, the Office Action states that "Pankhania teaches formulations that will release the active ingredient in the mouth, and the active ingredient will be absorbed through the oral or buccal mucosa." Applicants respectfully disagree with these conclusions.

PANKHANIA teaches the use of 50 to 800 mg of racemic ibuprofen in each dose (*see*, page 2, lines 28-31). These are high dosages related to a typical systemic application range. In contrast to PANKHANIA, the administration of low dosage anti-

inflammatory or anti-mycotic drug, as featured in claim 1, when used in buccal application, requires about 25 mg of ibuprofen per dosage (which then correlates to about 14.6 mg of racemic ibuprofen). Furthermore, the high dosages of ibuprofen used in the PANKHANIA composition, even when as little as the lowest 50 mg dosage, would recrystallize in the mouth environment and thus encounter the problems detailed in the comments above. The PANKHANIA composition would not work in a composition to be buccally administered and passively diffused into buccal and throat mucous membranes as recited in claim 1.

The oral mucosa is a lipophilic epithelium. Consequently, it is not possible for a lipophilic drug such as NSAID, in the formulations described in PANKHANIA to dissolve and coat the mucous without locally re-crystallizing. Applicants have applied a pharmacological rule, i.e., Fick's rule, to the claimed composition. This allows for local low dosage and mucous coating to obtain per-mucous absorption and bioavailability. The presently claimed composition will keep the lipophilic drug dissolved while being locally coated to the mucous, and without inducing any re-crystallization of the drug. The Office Action has failed to provide any scientific or clinical evidence to corroborate its contention that a formulation intended for oral administration, such as that described in PANKHANIA, would have these properties for passive diffusion into buccal and throat mucous membranes as recited in the present claims.

Again, while PANKHANIA mentions buccal administration, PANKHANIA fails to teach or suggest or disclose any use to locally treat this portion of the body, such as buccal mucous inflammation, sore throat, or local anti-mytotic therapy. PANKHANIA's goal is to treat migraine or nausea under a conventional oral route, and also a possible rectal, parenteral, or topical route, but fails to anticipate buccal administration.

In view of the above, PANKHANIA fails to provide an enabling disclosure with respect to the claimed subject matter. PANKHANIA does not enable one of ordinary skill in the art to make the claimed subject matter without undue experimentation. As such, PANKHANIA cannot serve as a reference to anticipate the composition of claim 1 and claims 2-8, 13-21 and 23-24 dependent thereon. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTIONS - 35 USC § 103

At page 7, item 17, the Office Action rejects claims 9-10 and 22 under 35 U.S.C. § 103(a) as being unpatentable over PANKHANIA, in view of MITRA (WO 95/07103). Applicants respectfully traverse the rejection.

Claims 9 and 10 are directed to a low dosage tablet according to claim 1, comprising a specific formulation. The formulation includes 25 mg of ibuprofen lysinate (claim 9) and 5 mg of ketoprofen lysinate (claim 10). As detailed above, the

claims include a composition to be buccally administered, wherein the composition is formulated to be passively diffused into buccal and throat mucous membranes. Claim 22 is directed to a method for treating buccopharyngeal ailments by local permucosal diffusion comprising administering the tablet according to claim 9.

MITRA relates to a systemic compound to be administered by an oral route, with general effects on the body and organs. Like PANKHANIA, MITRA fails to teach or suggest the buccal administration of a low dosage lipophilic anti-inflammatory or anti-mycotic drug that is passively diffused into buccal and throat mucous membranes. In addition, MITRA in combination with PANKHANIA fails to enable one of ordinary skill in the art to make or practice the claimed subject matter.

The Office Action relies on MITRA for teaching the use of specific amount of drugs (25 mg of ibuprofen lysinate and 5 mg of ketoprofen lysinate). The Office Action recognizes that MITRA discloses a composition with 50 to 800 mg ibuprofen lysinate and concludes that it would have been obvious to use this dosage in the PANKHANIA composition. Even the lowest dosage of 50 mg, however, is double the dosage of 25 mg recited in claim 9. Furthermore, as detailed in the above remarks, even the 50 mg ibuprofen amount when applied bucally, would provide local undesired re-crystallization. MITRA fails to teach or suggest anything to lead one of ordinary skill in the art to use the 25

mg dosage of ibupropen lysinate, instead of the higher dosage of 50 to 800 mg, to formulate a composition for buccal administration, as presently claimed.

For at least these reasons, the combination of PANKHANIA and MITRA fails to teach or suggest, and would not have rendered obvious, the low dosage tablets of claims 9 and 10, and the method of claim 22. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any

additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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